REMARKS

Claims 1-36 are currently pending; of these claims 19-36 are withdrawn from consideration. Claims 1-18 are currently under examination. Applicant believes that upon allowance of claim 1, claims 25-34 are to be rejoined with claim 1 and examined with it. Claims 25-34 recite methods of use of the specificity-determining substrate of claim 1.

Applicant gratefully acknowledges that rejection of claims 1-5, 7-15, and 17-18 under 35 U.S.C. 112, second paragraph, is withdrawn.

Applicant gratefully acknowledges that rejection of claims 4 and 13 under 35 U.S.C. 102(b) as being anticipated by Keyes is withdrawn.

The amendments to claims 1 and 10-14 related to complex formation with an elutable protein are supported in the specification at least at page 16, 4th paragraph; page 35, 5th paragraph; page 36, Table 8; page 41, 3rd paragraph; and page 43, Table 11.

The amendment to claims 1, 10, 25 and 33 reciting a "proteomic sample" is supported throughout the specification, and in particular at least at page 1, in the section Field of the Invention; page 3, 2nd paragraph; page 11, 5th paragraph of text; page 17, 1st paragraph; and the Examples.

The amendments to claims 7 and 16 are supported at least in claims 6 and 15 as originally filed.

The remaining amendments are made in order more particularly to point out and more distinctly to claim the subject matter that Applicant regards as his invention. It is believed that these amendments do not substantively narrow the subject matter recited in the claims.

ARGUMENT

A. Claims 6 and 15 are allowable under 35 U.S.C. 112, second paragraph.

Applicant has amended claims 6 and 15 to delete allegedly indefinite language specified in the Final Office Action. Consequently this rejection is considered moot. Applicant requests that this rejection be withdrawn at this time.

B. Claims 1-3, 5-6, 10-12, and 14-15 are novel under 35 U.S.C. 102(b) over Keyes.

Independent claim 1 is drawn in relevant part to a specificity-determining substrate wherein the specificity-determining substrate consists of a specificity-determining ligand bound to a support, wherein the specificity-determining substrate forms a complex in a homogenous fashion with a protein molecule comprised in a proteomic sample, and wherein the protein molecule is elutable from the complex, The transitional phrase "consists of" indicates that the specificity-determining substrate is constituted only of a support bonded to a specificity-determining ligand. The specificity-determining substrate has the properties that it forms a complex with a protein molecule comprised in a proteomic sample such that the protein molecule is elutable from the complex. The specification discloses that in proteomic separations a biological sample taken, by way of nonlimiting example, from cells or from a tissue, is disrupted to release all or a significant proportion of the total proteome present in the sample. The specificity-determining substrate of the claims is used to resolve the proteomic proteins into at least two subsets by contacting the sample with the specificity-determining substrate and collecting at least the flow-through (unbound) protein fraction and an elutable complexed protein fraction.

Claim 10 is drawn to a complex comprising a specificity-determining substrate described in claim 1 (see the preceding paragraph) and a protein molecule comprised in a proteomic sample. The protein molecule of the complex is elutable from the substrate.

The disclosure of Keyes is summarized in Applicant's Third Reply to the Nonfinal Office Action filed January 25, 2008, page 18, 3rd paragraph, incorporated herein by reference. Concerning independent claim 1, Keyes fails to disclose a specificity-determining substrate consisting only of a support bound to a specificity-determining ligand. Rather, the composition of Keyes that is asserted in the Final Office Action to read on the instant specificity-determining substrate is constituted of more than a support and a specificity-determining ligand. Furthermore, Keyes fails to disclose a composition that forms a complex with a protein molecule comprised in a proteomic sample. Keyes additionally fails to disclose that a protein molecule is elutable from any composition described in the reference. Keyes teaches only immobilization to a substrate (see at least Abstract; col. 7, lines 25 and 39-40; col. 8, lines 27, 32, and 59-60; col. 9, lines 29, 32, and 41; and claim 1).

Concerning claim 10, Keyes fails to disclose a complex that includes a) a specificity-determining substrate that consists only of a support bound to a specificity-determining ligand and b) an elutable protein molecule comprised in a proteomic sample.

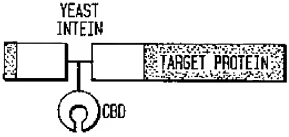
Analogous arguments apply, *mutatis mutandi*, to claims 11-13.

For all these reasons, Applicant submits that claims 1-3, 5-6, 10-12, and 14-15 are novel under 35 U.S.C. 102(b) over Keyes, and requests that this rejection be withdrawn.

C. Claims 1-6, 8-9, 10-15, and 17-18 are novel under 35 U.S.C. 102(b) over Comb et al.

The present claims are summarized above in section B, incorporated herein by reference.

The extensive disclosure of Comb et al. is summarized in Applicant's Third Reply to the Nonfinal Office Action filed January 25, 2008, page 19, 2nd paragraph, incorporated herein by reference. The Final Office Action has drawn attention in particular to Figure 32 of Comb et al. after having originally misidentified the figure referred to in the Nonfinal Office Action mailed January 5, 2007 as Figure 28. This error prevented Applicant from replying fully and substantively to the rejection originally imposed in the Nonfinal Office Action. Figure 32 discloses a synthetic tripartite fusion protein of which a central part includes a chitin binding domain (CBD) and the first and third parts include a cleavable peptide fragment and a cleavable target protein fragment (shaded portions), respectively (see extract from Fig. 32 of Comb et al.):



Concerning claim 1 (see Section B, above), Comb et al. fails to disclose that a specificity-determining substrate forms a complex with an elutable protein. In Fig. 32 of Comb et al. and the relevant disclosure in the patent, once the CBD of the fusion protein binds to a chitin substrate employed as an affinity column, the CBD remains bound to the chitin substrate and is

not eluted. Only fragments of the tripartite fusion protein are eluted; these fragments are not the same as "the" originally complexed protein molecule (claim 1) elutable from the complex.

Additionally Comb et al. fails to disclose that a protein molecule complexed with the specificity-determining substrate is comprised in a proteomic sample. Rather Comb et al. discloses only a transformed bacterial cell containing a vector encoding a genetically engineered fusion protein inducible by IPTG (col. 79, lines 42-54). Only the induced and overexpressed fusion protein forms a complex with a chitin substrate. In addition, the chitin-chitin binding domain pair constitutes an intentionally engineered specific binding pair designed to capture the fusion protein by affinity chromatography (col. 7, lines 21-23 and 64-67). Intentional engineering does not arise in a proteomic sample. Affinity chromatography is not a method useful in forming a complex with a protein molecule comprised in a proteomic sample.

Concerning claim 10, Comb et al. fails to disclose a complex comprising a specificity-determining substrate described in claim 1 (see Section B, above) and a protein molecule comprised in a proteomic sample, wherein the protein molecule is elutable from the substrate. The inapposite features of Comb et al. specified above with respect to claim 1 are incorporated herein by reference and apply to claim 10 equally. Further, in Comb et al. the CBD remains bound to a chitin substrate; additionally, only an induced genetically engineered fusion protein forms a complex with a chitin substrate.

Analogous arguments apply, *mutatis mutandi*, to claims 11-13.

Concerning claims 2-3 and 11-12 the chitin of the chitin-support composition of Comb et al. is not among the species enumerated in the claims, whether elected (succinyl group) or any other nonelected species. Chitin is a high molecular weight polymer prepared in Comb et al. by acetylation of chitosan supplied by Pfanstiehl Laboratories, after linking to a Sepharose substrate (col. 57, lines 15-62). For this additional reason claims 2-3 and 11-12 are novel over Comb et al.

Based on all these arguments, Applicant submits that claims 1-6, 8-9, 10-15, and 17-18 are novel under 35 U.S.C. 102(b) over Comb et al, and requests that this rejection be withdrawn.

D. Claims 1-18 are nonobvious under 35 U.S.C. 103(a) over Comb et al. in view of Margel.

The Final Office Action maintains rejection of claims 1-18 for obviousness over Comb et al. in view of Margel, even though the substance of the obviousness rejection is directed to the

purported prima facie obviousness of only claims 7 and 16 (Nonfinal Office Action, pages 6-7). The statement of rejection of claims 7 and 16 focuses on the solids content of the support being less than 8% (w/v) (Nonfinal Office Action, page 6, 9th paragraph).

In the absence of substantive grounds of rejection for obviousness of claims 1-6, 8-15, and 17-18, Applicant considers these claims to be nonobvious under 35 U.S.C. 103(a) on their face. Claims 1-6, 8-15, and 17-18 do not recite limitations drawn to solids content of the specificity-determining substrate and are thus free the cited prior art.

The deficiencies of Comb et al. as a reference have been identified in Section C, incorporated herein by reference.

The disclosure of Margel is summarized in Applicant's Third Reply to the Nonfinal Office Action filed January 25, 2008, page 20, 5th paragraph, incorporated herein by reference. Margel fails to provide the missing elements that are lacking in Comb et al.

Accordingly rejection of claims 7 and 16 under 35 U.S.C. 103(a) over Comb et al. in view of Margel is improper and cannot stand. Indeed, all of claims 1-18 are nonobvious over Comb et al. in view of Margel.

Applicant therefore requests that this rejection be withdrawn at this time.

E. Claims 1-18 are allowable under 35 U.S.C. 112, first paragraph as fulfilling the written description requirement.

Independent claim 1 has been amended to recite that the specificity-determining substrate forms a complex with a protein molecule comprised in a proteomic sample, wherein the protein molecule is elutable from the complex. Claims 10-13 have been amended to recite that the protein molecule is elutable from the substrate. These recitations are fully supported in the specification (see Remarks, above).

Accordingly, claims 1-18 fulfill the written description requirement. Applicant respectfully requests that this rejection be withdrawn at this time.

For the record, Applicant respectfully points out that this rejection is entirely improper. The rejection raises the false issue that the phrase "reversibly forms a complex with a protein molecule" is drawn to elution of inactive proteins. As is clear from elementary grammatical construction of "reversibly forms a complex with a protein molecule", the adverb "reversibly" modifies the verb form "bound". There is no reference in any claim recitation under

consideration at the time the Final Office Action was written that an adverb "reversibly" modifies a verb form relating to any notion of whether or not a protein is active or inactive. Applicant thus respectfully concludes that the Final Office Action raises a false issue, leading to a groundless rejection to be imposed. As noted, this rejection is now moot.

CONCLUSION

In this After Final Reply Applicant has striven to present amended claims that advance prosecution and that could not have been presented earlier because they respond to the Final Office Action. Applicant believes the amended claims are placed in condition for allowance, all pending rejections having been overcome.

Upon allowance of claim 1, Applicant respectfully requests that claims 25-34 be rejoined with claim 1. Claims 25-34 recite methods of use of the specificity-determining substrate of claim 1. Applicant requests that rejoined claims 25-34 be examined at this time by reopening prosecution.

Respectfully submitted,

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